High-Yield Formation of Substituted Tetracyanobutadienes from Reaction of Ynamides with Tetracyanoethylene.

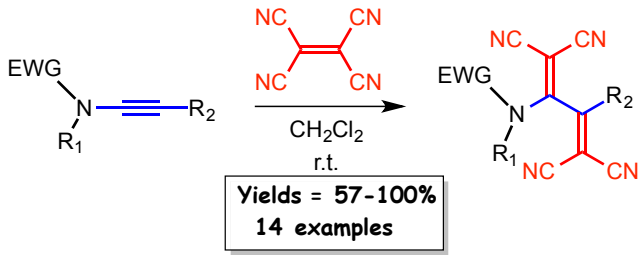
Marie Betou, Nicolas Kerisit, Esme Meledje, Yann R Leroux, Claudine Katan, Jean-François Halet, Jean-Claude Guillemin, Yann Trolez

Chem. Eur. J., 2014, 20, pp 9553–9557. doi:10.1002/chem.201402653

High-yield formation of substituted tetracyanobutadienes from reaction of ynamides with tetracyanoethylene

Marie Betou,[a] Nicolas Kerisit,[a] Esme Meledje,[a] Yann R. Leroux,[b] Claudine Katan,[b] Jean-François Halet,[b] Jean-Claude Guillemin[a] and Yann Trolez*[a]

Table of content: Reaction between ynamides and tetracyanoethylene at room temperature in dichloromethane provides tetracyanobutadienes in good to quantitative yields, following a sequence of [2+2]cycloaddition-retroelectrocyclization.



Abstract: The high-yield sequence of [2+2]cycloaddition-retroelectrocyclization of ynamides with tetracyanoethylene (TCNE) is described. The reaction provided tetracyanobutadiene (TCBD) species, which were characterized by various techniques. DFT and TD-DFT calculations were also performed to complement experimental findings.

Keywords: Ynamides, tetracyanoethylene, [2+2]cycloaddition, tetracyanobutadienes

The sequence of [2+2]cycloaddition-retroelectrocyclization (CA-RE) between tetracyanoethylene (TCNE) and alkynyl-transition metal complexes has been known for several decades[1] and has extensively been studied.[2] However, to the best of our knowledge, this reactivity with purely organic alkynes has been discovered only in 1999 with α-substituted thienylalkynes.[3] Since then, other alkynes substituted by electron-donating groups (EDG) have been shown to react the same way (Figure 1).[4] This reaction has mostly been popularized by Diederich and co-workers for the last decade.[5] Aniline-,[6] azulene-[7] and heteroazulene-substituted[8] alkynes represent the best examples of this reaction by providing yields over 90%, by simply mixing the two reactants together in a solvent at room temperature. However, the reactivity of TCNE with alkynes directly substituted by an electron donating heteroatom has never been described.

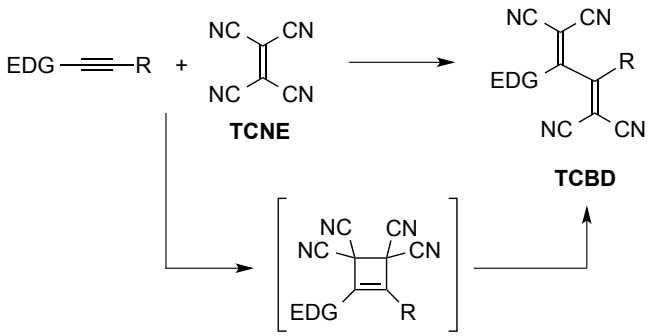


Figure 1. Previous work on [2+2]cycloaddition of TCNE with electron-rich alkynes.

As examples of such compounds, ynamides have received considerable attention during the last

decade.[9] This interest can be explained by the new efficient synthetic methodologies recently developed.[10] The ynamide C-C triple bond is activated by the donating ability of the nitrogen atom (Figure 2). However, unlike ynamines, these compounds are stabilized by an electron-withdrawing group (EWG) on the nitrogen, which makes them air-stable and thus easy to handle. [2+2]Cycloadditions of ynamides are known and usually require a catalyst[11] or a Lewis acid,[12] except for their reaction with the ketene.[13]

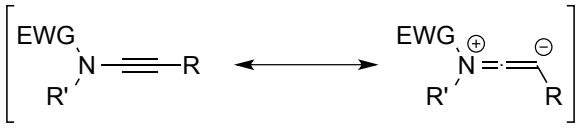
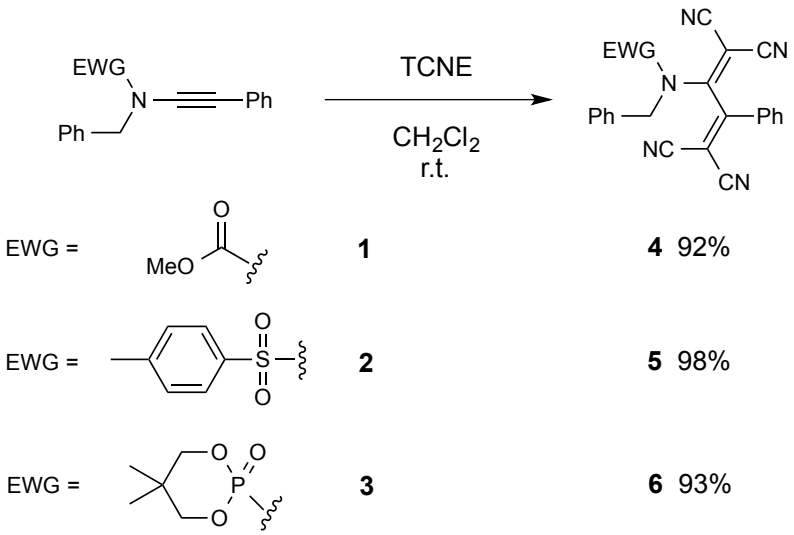


Figure 2. Ynamide mesomeric forms highlighting the electron richness of the C-C triple bond.

In this communication, we report on the reactivity of a variety of ynamides with TCNE to achieve tetracyanobutadiene (TCBD) species in moderate to excellent yields (57% to quantitative) at room temperature and without the need for any activating agent.

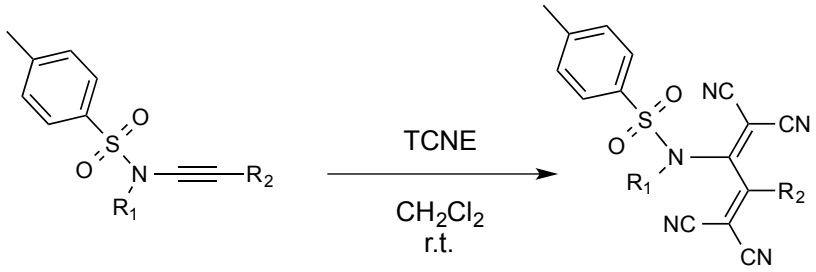
At first, three different ynamides, which differ from each other by the nature of the electron-withdrawing group, were synthesized. Ynamides **1** and **2** (Scheme 1) were prepared according to literature procedures[14] whereas the synthesis of **3** has been inspired by a recent article from the Hsung group (see Supporting Information for details).[15] Compounds **1**-**3** in dichloromethane were reacted with an equimolar amount of TCNE at room temperature overnight. The same reactivity was observed and TCBD adducts **4**, **5** and **6** were obtained in 92, 98 and 93% yield, respectively.‡ This reaction is supposed to proceed according to a sequence of [2+2]CA-RE as described in Figure 1.



Scheme 1. Reactivity of ynamides **1-3** with TCNE giving the corresponding TCBD adducts **4**-**6** in excellent yields.

Secondly, the scope of the reaction was investigated using the tosylate group. This EWG was preferred over the carbamate and the phosphonate due to its ease of preparation and higher degree of crystallinity.

Table 1. Scope of the [2+2]CA-RE of ynamides and TCNE.



Entry	Ynamide	TCBD	Yield
1	**7** (R_1=CH_3, R_2=Ph)	**17**	100%
2	**8** (R_1=CH_2CH_2Ph, R_2=Ph)	**18**	95%
3	**9** (R_1=CH_2Ph, R_2=*p*-Cl-C_6H_4)	**19**	90%
4	**10** (R_1=CH_2Ph, R_2=*p*-MeO-C_6H_4)	**20**	100%
5	**11** (R_1=CH_2Ph, R_2=*p*-NC-C_6H_4)	**21**	57%[a]
6	**12** (R_1=CH_2Ph, R_2=*p*-Ph_2N-C_6H_4)	**22**	92%
7	**13** (R_1=CH_2Ph, R_2=H)	**23**	100%
8	**14** (R_1=CH_2Ph, R_2=*n*hexyl)	**24**	100%
9	**15** (R_1=CH_2Ph, R_2=pyridin-3-yl)	**25**	58%[b]
10	**16** (R_1=CH_2Ph, R_2=thiophen-2-yl)	**26**	87%

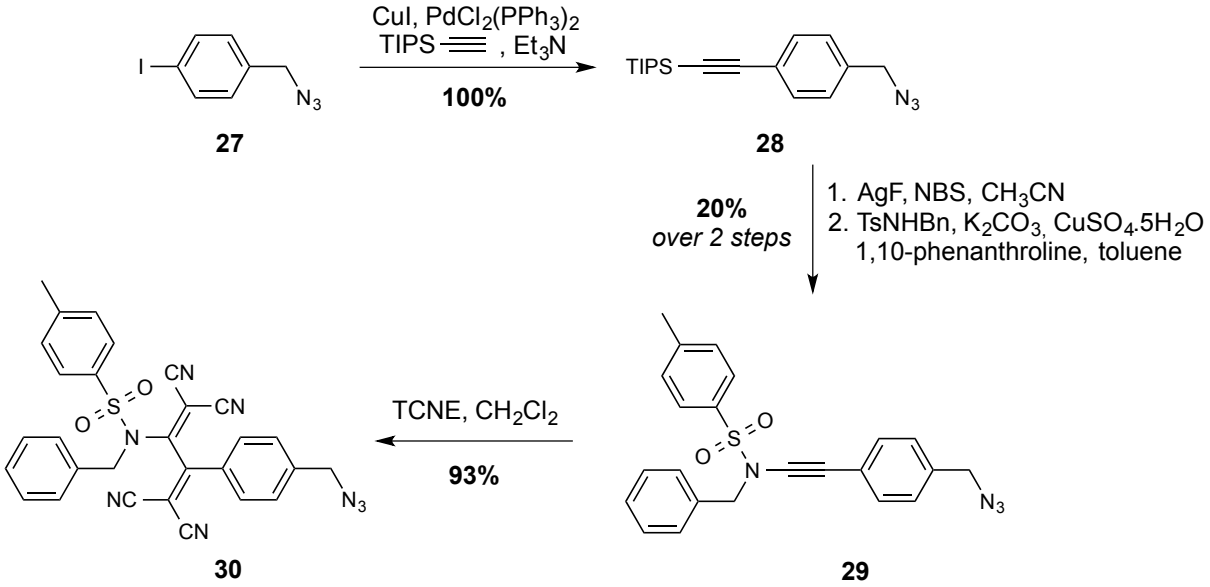
[a] using 2 eq. of TCNE, the yield was increased to 79%; [b] 2 eq. of TCNE were used in that case, because when using 1 eq. of TCNE, an inseparable 1.8:1.0 mixture of **15:25** was obtained; when 3 eq. of TCNE were used over 64 h, **25** was obtained in 75% yield.

Ynamides **7**-**16** were synthesized according to Evano's[10c, 16] or Hsung's[14a] procedures. The influence of the second group linked to the nitrogen (R_1 in Table 1) was first evaluated by turning it into a methyl or a homobenzylic group (entries 1 and 2). No dramatic change was observed, the yield of the reaction remaining excellent (95% to quantitative). The influence of the group linked to the C-C triple bond was also evaluated. Electron-rich phenyl groups (*p*-methoxyphenyl and *p*-diphenylaniline, entries 4 and 6) did not change the yield (quantitative and 92% respectively). However, electron-poor phenyl groups (*p*-chlorophenyl and *p*-cyanophenyl, entries 3 and 5) slightly to moderately decreased the reactivity (90% and 57% respectively). Nevertheless, particularly noteworthy is the significant increase of the yield with *p*-cyanophenyl group when using 2 equivalents of TCNE instead of 1 (from 57% to 79%). The *n*-hexyl group or a hydrogen in lieu of a phenyl one provided TCBD in quantitative yields (entries 7 and 8). Heteroaromatic substituents were also studied: Whereas a thiophen-2-yl group did not really affect the yield of the reaction (87%, entry 10), a pyridin-3-yl group significantly decreased the yield to 58%, even using 2 equivalents of TCNE. Indeed, 3 equivalents of TCNE and a longer reaction time of 64 h were necessary to give **25** in 75% yield. In every instance, when the yield was not over 90%, the conversion was not complete. It was never due to decomposition during the purification process.

From these figures, we can draw the conclusion that only electron-poor groups might significantly decrease the yield of the reaction in some particular cases but remain very well tolerated.

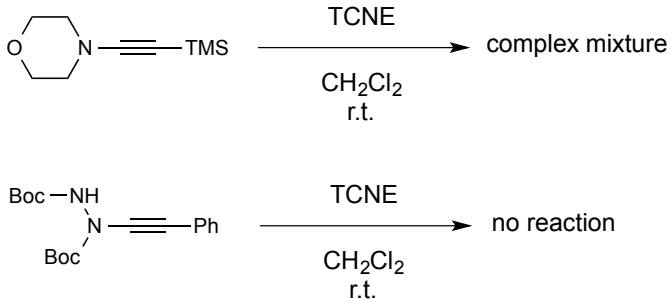
In addition, ynamide **29**, bearing an azide functional group, was synthesized in 19% yield over 3 steps starting from the known azide **27** (Scheme 2).[17] A Sonogashira coupling using (triisopropylsilyl)acetylene gave the protected alkyne **28** in quantitative yield and the latter was then reacted with silver fluoride and *N*-bromosuccinimide.[18] The formed bromide derivative formed was

unstable, and was further reacted under Hsung's reaction condition to afford ynamide **29**. Reaction with one equivalent of TCNE gave TCBD **30** in an excellent 93% yield. This azide-functionalized TCBD **30** allows us to envisage further incorporation of new functional groups by Copper-catalyzed Azide-Alkyne Cycloaddition (CuAAC) reaction[19] for instance, as it was performed in the past with other related TCBDs.[20]



Scheme 2. Synthesis of ynamide **29** and further reactivity to form TCBD **30**.

This reactivity does not seem to be a general property of *N*-substituted alkynes but a particularity of ynamides. Indeed, when reacting the commercially available ynamine **31** with TCNE using the same procedure as described above, a complex mixture of inseparable colored products was obtained, probably resulting from the over reaction of this very reactive compound, as it has already been described in the literature with other related compounds.[21] By contrast, when ynehydrazide **32** [22] was reacted with TCNE, no reaction occurred. In each case, no TCBD could be isolated. These observations led us to conclude that the right balance was found with ynamides for the reaction with TCNE to yield TCBD in high yields.



Scheme 3. Reactivity of an ynamine and an ynehydrazide with TCNE.

Products **4**-**6** and **17**-**26** were characterized by ^{1}H- and ^{13}C-NMR spectroscopy, mass spectrometry, UV-vis spectroscopy and electrochemistry. Additionally, compounds **4**, **5**, **17**, **19**-**22** and **25** were also characterized by X-ray diffraction, confirming unambiguously the structure of the adducts synthesized (Figure 3 and S1-S10). X-ray structures of compounds **4**-**5**, **17**, **19**, **20**-**22** and **25** reveal

highly distorted TCBD groups with significant twist between the two dicyanovinyl planes (Figure 3). Indeed, the torsion angle between these groups ~~is comprised~~ ranges between 56° and 68°, except for compound **17** the torsion angle of which is 110°. The s-*cis* conformation in the solid state is consistent with that reported for TCBD analogs.[4a, 23] DFT optimized geometries both in vacuum and in solvents, suggest that the s-*cis* conformation is preferred in solution even though the difference with the s-*trans* conformation stays within a few hundreds of eV (Table S2). Both experiment and calculations evidence clearly a single bond character of the central C-C bond of the TCBD group (Table S1).

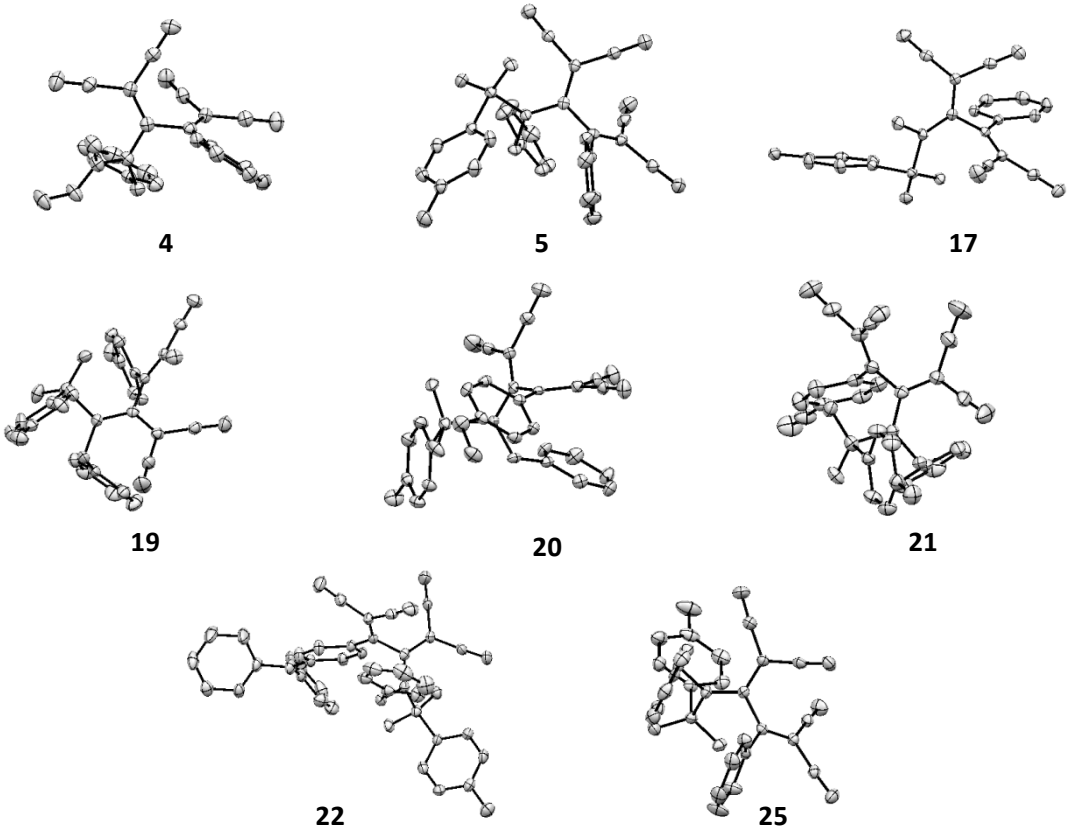


Figure 3. X-ray structures of compounds **4**, **5**, **17**, **19**-**22** and **25**. Solvent and hydrogen atoms are omitted for clarity.

UV-vis absorption spectra are shown in Figures 4 and S11-S16. Except for the donor-substituted compounds, they reveal two broad absorption bands in the UV range at *ca* 340 nm and *ca* 260 nm with little solvatochromism indicative of non-polar ground states. TD-DFT calculations and tentative deconvolution of these optical spectra show that several electronic transitions contribute to each band (Figure S15 and Table S5). Moreover, neither the HOMO nor the HOMO-1 (Table S3) are involved in these transitions leading to the absence of absorption in the visible spectrum. Indeed, natural transition orbital[24] plots reveal the electronic redistributions upon excitation that mainly involve the dicyanovinyl moiety connected to the phenyl ring for the first band and the other dicyanovinyl group for the second one (Table S5). Significant red shift occurs upon donor substitution with appearance of a clear isolated band in the visible range for the strongest donor (compound **22**) (Figure 4). Comparison of molecular (Table S4) and transition (Table S6) orbitals of compound **22** reveal the HOMO->LUMO nature of this band, while higher-lying bright states show good correspondence with those discussed for compounds lacking donor substitution. Compounds **20** and **26** show an intermediary behavior due to smaller splittings between the first two excited states

(Table S6).

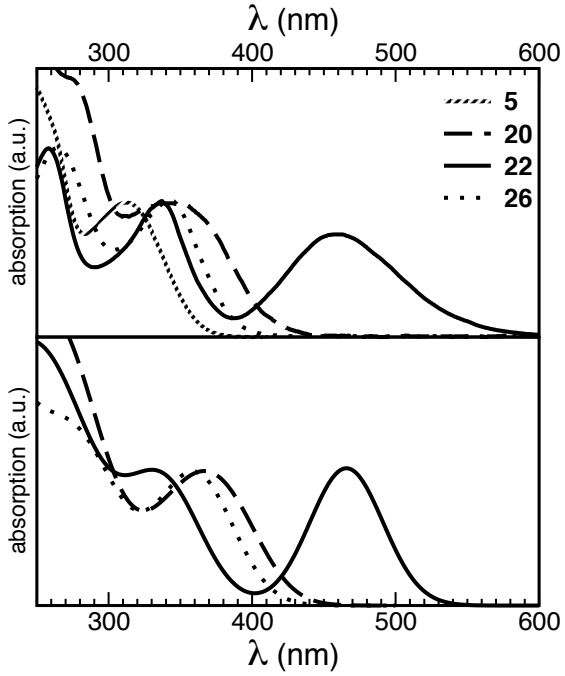


Figure 4. Experimental (top) and calculated (bottom) normalized UV-vis absorption spectra of compounds **5**, **20**, **22** and **26** in CH_2Cl_2. To ensure easy comparison, calculated data have been shifted by an overall offset of 0.36 eV.

In order to investigate the electronic properties of these new TCBD compounds, cyclic voltammetries were recorded in acetonitrile (Figure S17). Two distinct reversible one-electron reduction waves can be observed at approximately -0.5 and -1.0 V vs Fc^+/Fc (Table 2) that may be assigned to the subsequent reduction of the two dicyanovinyl groups. Moreover, these TCBD species are among the easiest ones to reduce out of such adducts according to the literature[4a, 23], making them potential super-acceptors. From these values were deduced the two electronic affinities (Table 2) for each compound (see Supporting Information for details).[25] In addition, no oxidation could be observed (except for compound **22**), in major contrast with other examples of adducts from reaction of TCNE with electron rich alkynes.[6a, 7a, 8]

Table 2. Measured half-wave potentials ($E_{1/2}$) and electronic affinities (EA) of compounds **4**-**6**, **20**, **22** and **26** calculated on the basis of cyclic voltammetry. Acetonitrile solution of 0.1 $mol.L^{-1}$ of nBu_4NPF_6 and 10^{-3} $mol.L^{-1}$ of TCBD at 100 $mV.s^{-1}$. DFT calculated values ($EA^{i,cal}$) obtained at B3LYP/6-31+G* level in acetonitrile are also reported.

Compounds	**4**	**5**	**6**	**20**	**22**	**26**
$E_{1/2}^1$ (V vs Fc^+/Fc)	-0.52	-0.54	-0.62	-0.58	-0.60	-0.52
$E_{1/2}^2$ (V vs Fc^+/Fc)	-1.06	-1.00	-1.04	-1.02	-1.01	-0.93
EA^1 (eV)	4.32	4.29	4.21	4.26	4.24	4.31
$EA^{1,cal}$ (eV)	*4.54*	*4.50*	*4.37*	*4.44*	*4.28**	*4.46*
EA^2 (eV)	3.77	3.83	3.78	3.81	3.81	3.90
$EA^{2,cal}$ (eV)	*3.69*	*3.71*	*3.85*	*3.70*	*3.71**	*3.82*

* values derived from total electronic energies instead of Gibbs free energies

From a theoretical point of view, calculated adiabatic electron affinities correlate nicely with the experimental values given in Table 2. Electron affinities are only slightly affected by the substitutions

implemented in this work, the lowest value being observed with the strongest donor group (compound **22**). Optimized geometries of anions evidence sizeable diminution of both the dihedral angle and the C-C bond length between the two dicyanovinyl groups consistently with the orbital structure of the LUMO (Tables S3 and S4). This is even more pronounced for di-anions and indicates electron removal from orbitals delocalized over the whole TCBD unit. Moreover, except for **22**, calculated adiabatic ionization energies in acetonitrile amount to *ca* 7 eV (Tables S7 and S9), reaching almost that of benzene. For the unsubstituted compounds, this is consistent with a HOMO mainly localized on the benzyl ring (Table S3) leading to an increased bond length alternation in their cationic forms (Table S8). Such high oxidation potentials explain that no oxidation could be observed by cyclic voltammetry in these conditions.

To conclude, an original reactivity between fourteen different ynamides and TCNE has been described. It allows for the formation of new TCBD species in good to quantitative yields by simply mixing equimolar quantities of ynamides and TCNE in dichloromethane at room temperature. These new compounds were characterized by various techniques and their properties were explained by TD-DFT calculations. In this communication, the nature of all the different functional groups of the ynamides has been investigated bringing us to the conclusion that only a strong electron-withdrawing group linked to the C-C triple bond can affect the yield of the reaction. Moreover, this reactivity paves the way to the construction of more sophisticated systems that could exhibit interesting properties for new materials in opto-electronic devices.

Notes and references

[a] *Ecole Nationale Supérieure de Chimie de Rennes, Institut des Sciences Chimiques de Rennes, UMR 6226, CNRS, 11 allée de Beaulieu, CS 50837, 35708 Rennes Cedex 7, France. Fax: 33 2 23 23 81 08; Tel: 33 2 23 23 80 69; E-mail: yann.trolez@ensc-rennes.fr*

[b] *Institut des Sciences Chimiques de Rennes, Université de Rennes 1, CNRS, UMR 6226, Campus de Beaulieu, 35042 Rennes Cedex, France.*

† Electronic Supplementary Information (ESI) available: synthetic procedure and characterization of compounds **3**-**6, 12, 17-30**; electrochemical analysis; computational details and results. CCDC reference numbers of compounds **3**, **4, 5, 17, 19, 20, 21, 22** and **25**: 905007, 881967, 884433, 960613, 962305, 962971, 962979, 966740, 976260 respectively. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/b000000x/

‡ Typical experimental procedure for the formation of TCBD compounds: A solution of ynamide (1.0 eq.) and tetracyanoethylene (1.0 eq.) in CH_2Cl_2 (0.1 M) was stirred at room temperature overnight. The solvent was evaporated, and if needed the residue was subjected to chromatography on silica gel, to afford TCBD moieties.

Acknowledgements

The authors gratefully acknowledge Dr. L. Toupet from Institut de Physique de Rennes for solving X-ray structures, T. C. Nguyen for help in performing DFT calculations and Pr. A. Boucekkine for useful discussions. This work was granted access to the HPC resources of CINES and of IDRIS under the allocations 2012-[x2012080649] and 2013-[x2013080649] made by GENCI (Grand Equipement National de Calcul Intensif). N. K. acknowledges a PhD fellowship from the French Ministry of Research. M. B. thanks the Région Bretagne for a post-doctoral grant.

References

[1] M. I. Bruce, J. R. Rodgers, M. R. Snow, A. G. Swincer, *J. Chem. Soc., Chem. Commun.* **1981**, 271-272.

[2] M. I. Bruce, *Aust. J. Chem.* **2011**, *64*, 77-103.

[3] a) X. Wu, J. Wu, Y. Liu, A. K. Y. Jen, *J. Am. Chem. Soc.* **1998**, *121*, 472-473; b) C. Cai, I. Liakatas, M.-S. Wong, M. Bösch, C. Bosshard, P. Günter, S. Concilio, N. Tirelli, U. W. Suter, *Org. Lett.* **1999**, *1*, 1847-1849.

[4] a) T. Mochida, S. Yamazaki, *J. Chem. Soc., Dalton Trans.* **2002**, 3559-3564; b) Y. Morioka, N. Yoshizawa, J.-i. Nishida, Y. Yamashita, *Chem. Lett.* **2004**, *33*, 1190-1191; c) S.-i. Kato, M. Kivala, W. B. Schweizer, C. Boudon, J.-P. Gisselbrecht, F. Diederich, *Chem. Eur. J.* **2009**, *15*, 8687-8691; d) D. Koszelewski, A. Nowak-Król, D. T. Gryko, *Chem. Asian J.* **2012**, *7*, 1887-1894; e) R. García, M. Á. Herranz, M. R. Torres, P.-A. Bouit, J. L. Delgado, J. Calbo, P. M. Viruela, E. Ortí, N. Martín, *J. Org. Chem.* **2012**, *77*, 10707-10717.

[5] a) S.-i. Kato, F. Diederich, *Chem. Commun.* **2010**, *46*, 1994-2006; b) B. Breiten, M. Jordan, D. Taura, M. Zalibera, M. Griesser, D. Confortin, C. Boudon, J.-P. Gisselbrecht, W. B. Schweizer, G. Gescheidt, F. Diederich, *J. Org. Chem.* **2013**, *78*, 1760-1767.

[6] a) T. Michinobu, J. C. May, J. H. Lim, C. Boudon, J.-P. Gisselbrecht, P. Seiler, M. Gross, I. Biaggio, F. Diederich, *Chem. Commun.* **2005**, 737-739; b) X. Tang, W. Liu, J. Wu, C.-S. Lee, J. You, P. Wang, *J. Org. Chem.* **2010**, *75*, 7273-7278.

[7] a) T. Shoji, S. Ito, K. Toyota, M. Yasunami, N. Morita, *Chem. Eur. J.* **2008**, *14*, 8398-8408; b) T. Shoji, E. Shimomura, M. Maruyama, A. Maruyama, S. Ito, T. Okujima, K. Toyota, N. Morita, *Eur. J. Org. Chem.* **2013**, *2013*, 7785-7799.

[8] T. Shoji, J. Higashi, S. Ito, T. Okujima, M. Yasunami, N. Morita, *Chem. Eur. J.* **2011**, *17*, 5116-5129.

[9] a) G. Evano, A. Coste, K. Jouvin, *Angew. Chem. Int. Ed.* **2010**, *49*, 2840-2859; b) K. A. DeKorver, H. Li, A. G. Lohse, R. Hayashi, Z. Lu, Y. Zhang, R. P. Hsung, *Chem. Rev.* **2010**, *110*, 5064-5106.

[10] a) M. O. Frederick, J. A. Mulder, M. R. Tracey, R. P. Hsung, J. Huang, K. C. M. Kurtz, L. Shen, C. J. Douglas, *J. Am. Chem. Soc.* **2003**, *125*, 2368-2369; b) T. Hamada, X. Ye, S. S. Stahl, *J. Am. Chem. Soc.* **2008**, *130*, 833-835; c) A. Coste, G. Karthikeyan, F. Couty, G. Evano, *Angew. Chem. Int. Ed.* **2009**, *48*, 4381-4385.

[11] N. Riddell, K. Villeneuve, W. Tam, *Org. Lett.* **2005**, *7*, 3681-3684.

[12] a) K. C. M. Kurtz, R. P. Hsung, Y. Zhang, *Org. Lett.* **2006**, *8*, 231-234; b) L. You, Z. F. Al-Rashid, R. Figueroa, S. K. Ghosh, G. Li, T. Lu, R. P. Hsung, *Synlett* **2007**, 1656-1662.

[13] a) A. L. Kohnen, X. Y. Mak, T. Y. Lam, J. R. Dunetz, R. L. Danheiser, *Tetrahedron* **2006**, *62*, 3815-3822; b) Y.-P. Wang, R. L. Danheiser, *Tetrahedron Lett.* **2011**, *52*, 2111-2114.

[14] a) Y. Zhang, R. P. Hsung, M. R. Tracey, K. C. M. Kurtz, E. L. Vera, *Org. Lett.* **2004**, *6*, 1151-1154; b) C.-F. Xu, M. Xu, Y.-X. Jia, C.-Y. Li, *Org. Lett.* **2011**, *13*, 1556-1559.

[15] K. A. DeKorver, M. C. Walton, T. D. North, R. P. Hsung, *Org. Lett.* **2011**, *13*, 4862-4865.

[16] K. Jouvin, A. Coste, A. Bayle, F. Legrand, G. Karthikeyan, K. Tadiparthi, G. Evano, *Organometallics* **2012**, *31*, 7933-7947.

[17] J. Lee, S.-U. Kang, J.-O. Lim, H.-K. Choi, M.-k. Jin, A. Toth, L. V. Pearce, R. Tran, Y. Wang, T. Szabo, P. M. Blumberg, *Bioorg. Med. Chem.* **2004**, *12*, 371-385.

[18] T. Lee, H. R. Kang, S. Kim, S. Kim, *Tetrahedron* **2006**, *62*, 4081-4085.

[19] a) V. V. Rostovtsev, L. G. Green, V. V. Fokin, K. B. Sharpless, *Angew. Chem. Int. Ed.* **2002**, *41*, 2596-2599; b) C. W. Tornøe, C. Christensen, M. Meldal, *J. Org. Chem.* **2002**, *67*, 3057-3064.

[20] Y. Li, T. Michinobu, *Polym. Chem.* **2010**, *1*, 72-74.

[21] G. Jayamurugan, J.-P. Gisselbrecht, C. Boudon, F. Schoenebeck, W. B. Schweizer, B. Bernet, F. Diederich, *Chem. Commun.* **2011**, *47*, 4520-4522.

[22] R. E. Beveridge, R. A. Batey, *Org. Lett.* **2012**, *14*, 540-543.

[23] T. Michinobu, C. Boudon, J.-P. Gisselbrecht, P. Seiler, B. Frank, N. N. P. Moonen, M. Gross, F. Diederich, *Chem. Eur. J.* **2006**, *12*, 1889-1905.
[24] R. L. Martin, *J. Chem. Phys.* **2003**, *118*, 4775-4777.
[25] a) J. L. Bredas, R. Silbey, D. S. Boudreaux, R. R. Chance, *J. Am. Chem. Soc.* **1983**, *105*, 6555-6559; b) S. Trasatti, *J. Electroanal. Chem. Interfacial Electrochem.* **1983**, *150*, 1-15; c) Q. Xie, S. Kuwabata, H. Yoneyama, *J. Electroanal. Chem.* **1997**, *420*, 219-225.